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Terms	Documents
((IL-2 or interleukin-2) and (cancer or tumor or tumour)).clm. and (anergic or anergy)	16

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USPT	((IL-2 or interleukin-2) and (cancer or tumor or tumour)).clm. and (anergic or anergy)	16	L21
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USPT	(IL-2 or interleukin-2) and ((anergy or anergic) same (inhibit or inhibition or overcome or block or prevent or preventing or prevention or suppress$))	161	L19
USPT	(IL-2 or interleukin-2) and (anergy or anergic)	303	L18
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USPT	(inhibit or inhibition or prevent or prevention or block) same anergy and method.clm.	74	L10
USPT	(inhibit or inhibition or prevent or prevention or block) same anergy	113	L9
USPT	(inhibit or inhibition or prevent or preventio or block) same anergy	110	L8
USPT	cytokine same gamma same anergy	10	L7
USPT	BOUSSIOTIS-Vassiliki-A.in.	0	L6
USPT	BOUSSIOTIS-V-A.in.	0	L5
DWPI	BOUSSIOTIS-V-A.in.	4	L4
DWPI	(gamma and cytokine).ti.	11	L3
DWPI	(modulating and gamma and cytokine).ti	18	L2
DWPI	Boussiotis-vassiliki-A.in.	0	L1

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1: Becker JC, Brocker EB. R

Prevention of anergy induction in cloned T cells by interleukin 12.
Exp Dermatol. 1994 Dec;3(6):283-9.
PMID: 7538408 [PubMed - indexed for MEDLINE]

2: Parmiani G. R

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Immunol Today. 1993 Nov;14(11):536-8. Review.
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3: Boussiotis VA, Lee BJ, Freeman GJ, Gribben JG, Nadler LM. R

Induction of T cell clonal anergy results in resistance, whereas CD28-mediated costimu
for susceptibility to Fas- and Bax-mediated programmed cell death.
J Immunol. 1997 Oct 1;159(7):3156-67.
PMID: 9317113 [PubMed - indexed for MEDLINE]

4: Boussiotis VA, Freeman GJ, Berezovskaya A, Barber DL, Nadler LM. R

Maintenance of human T cell anergy: blocking of IL-2 gene transcription by activated
Science. 1997 Oct 3;278(5335):124-8.
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5: Boussiotis VA, Freeman GJ, Gribben JG, Nadler LM. R

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6: Boussiotis VA, Barber DL, Nakarai T, Freeman GJ, Gribben JG, Bernstein GM, D'Andrea AD, Ritz J, Nadler LM. R

Prevention of T cell anergy by signaling through the gamma c chain of the IL-2 recepto
Science. 1994 Nov 11;266(5187):1039-42.
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7: Weissman IL. R

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Jpn J Cancer Res. 1994 Oct;85(10):inside front cover. Review. No abstract available.
PMID: 7961100 [PubMed - indexed for MEDLINE]

☐ **8**: Grundstrom S, Dohlsten M, Sundstedt A. R

IL-2 unresponsiveness in anergic CD4+ T cells is due to defective signaling through the gamma-chain of the IL-2 receptor.
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☐ **9**: Kaufman M, Andris F, Leo O. Free in PMC, R

A logical analysis of T cell activation and anergy.
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PMID: 10097134 [PubMed - indexed for MEDLINE]

☐ **10**: Schwartz RH. R

Models of T cell anergy: is there a common molecular mechanism?
J Exp Med. 1996 Jul 1;184(1):1-8. Review. No abstract available.
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☐ **11**: Quill H. R

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J Immunol. 1996 Feb 15;156(4):1325-7. Review. No abstract available.
PMID: 8568229 [PubMed - indexed for MEDLINE]

☐ **12**: Selliah N, Finkel TH. R

Cutting edge: JAK3 activation and rescue of T cells from HIV gp120-induced unrespo
J Immunol. 1998 Jun 15;160(12):5697-701.
PMID: 9637477 [PubMed - indexed for MEDLINE]

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Differential association of protein tyrosine kinases with the T cell receptor is linked to of anergy and its prevention by B7 family-mediated costimulation.
J Exp Med. 1996 Aug 1;184(2):365-76.
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☐ **14**: Boussiotis VA, Freeman GJ, Gribben JG, Nadler LM. R

The critical role of CD28 signalling in the prevention of human T-cell anergy.
Res Immunol. 1995 Mar-Apr;146(3):140-9. Review. No abstract available.
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☐ **15**: Heeg K, Gaus H, Griese D, Bendigs S, Miethke T, Wagner H. R

Superantigen-reactive T cells that display an anergic phenotype in vitro appear functio
Int Immunol. 1995 Jan;7(1):105-14.
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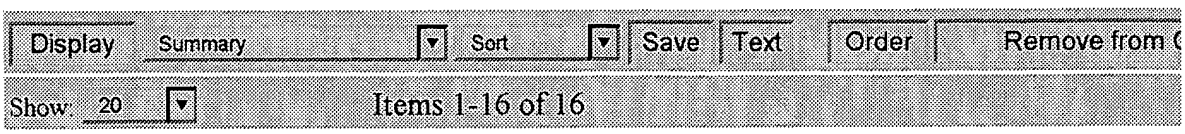
☐ **16**: Li XC, Demirci G, Ferrari-Lacraz S, Groves C, Coyle A, Malek TR, Strom TB. R

IL-15 and IL-2: a matter of life and death for T cells in vivo.
Nat Med. 2001 Jan;7(1):114-8.
PMID: 11135625 [PubMed - indexed for MEDLINE]



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	#6	Link to **PubMed** from (**9311917**)	09:02:16	200
	#4	Search **nadler lm**	09:00:39	213
	#1	Search **anergic and stimulate**	08:57:00	35

Clear History

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egin 55,72,154,399,351

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            $0.00    0.002 Hrs File410
     $0.00  Estimated cost File410
     $0.00  Estimated cost this search
     $0.03  Estimated total session cost   0.004 Hrs.

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? s anti(w)gamma(w)chain and cytokine?

          766498  ANTI
          516643  GAMMA
          678765  CHAIN
              45  ANTI(W)GAMMA(W)CHAIN
          206812  CYTOKINE?
      S1       0  ANTI(W)GAMMA(W)CHAIN AND CYTOKINE?
? s (gamma(w)chain)(20n)(antibod?) and cytokine?

          516643  GAMMA
          678765  CHAIN
         1006840  ANTIBOD?
             532  GAMMA(W)CHAIN(20N)ANTIBOD?
          206812  CYTOKINE?
      S2      25  (GAMMA(W)CHAIN)(20N)(ANTIBOD?) AND CYTOKINE?
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? t s3/7/all


 3/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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13365401     BIOSIS Number: 99365401
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Interleukin-15 triggers the proliferation and cytotoxicity of granular lymphocytes in patients with lymphoproliferative disease of granular lymphocytes

Zambello R; Facco M; Trentin L; Sancetta R; Tassinari C; Perin A; Milani A; Pizzolo G; Rodeghiero F; Agostini C; Meazza R; Ferrini S; Semenzato G
Univ. Padova, Dip. Med. Clin. Sperimentale, Via Giustiniani 2, 35128 Padova, Italy

Blood 89 (1). 1997. 201-211.
Full Journal Title: Blood
ISSN: 0006-4971
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 004 Ref. 053279

The recently cloned **cytokine** interleukin-15 (IL-15) shares several functional activities with IL-2 in different cell systems. Although IL-15 does not show sequence homology with IL-2, it uses components of the IL-2 receptor (IL-2R) for binding and signal transduction, namely, p75 (beta) and the p64 (gamma) chains of IL-2R. To evaluate whether IL-15 is involved in the activation of granular lymphocytes (GL) in patients with lymphoproliferative disease of granular lymphocytes (LDGL), we evaluated the ability of IL-15 to stimulate GL proliferation, cytotoxic function, and the role of IL-2R beta and gamma molecules on relevant cells. Our results show that IL-15 stimulates cell proliferation and cytotoxic activity of GL in LDGL patients. Reverse-transcriptase polymerase chain reaction (RT-PCR) and phenotypic analyses using the anti-IL-2R **gamma-chain** -specific TUGh4 monoclonal **antibody** (MoAb) indicate that both CD3+ and CD3- GL express the p64 IL-2R, a result previously unknown. IL-15 activity was inhibited by antibodies against p75 and p64 IL-2R chains, while no inhibitory effects are detectable with anti-p55 IL-2R antibody. The association of anti-p75 and anti-p64 IL-2R MoAbs resulted in a nearly complete (95%) inhibition of IL-15-induced GL proliferation. Using RT-PCR analysis, we demonstrated that highly purified CD3+ and CD3- GL did not express mRNA for IL-15 or IL-2. By contrast, a clear-cut IL-15 mRNA signal was detected by RT-PCR in patients' peripheral blood mononuclear cells, with monocytes likely accounting for the source of IL-15 in LDGL patients. However, even in concentrated supernatants from enriched monocyte populations, we could not demonstrate the presence of IL-15 protein. Using anti-IL-15 specific MoAbs, a membrane-bound form of this **cytokine** was demonstrated both on CD3+ and CD3- LDGL cells. By RT-PCR analysis, purified GL from these patients were found to express the message for IL-15 receptor a chain. Taken together, these results indicate that both CD3+ and CD3- GL are stimulated by IL-15 and that this **cytokine** mediates its activity through the beta and gamma chains of the IL-2R, providing further suggestions for the interpretation of the mechanisms that lead to cell expansion in patients with LDGL.

3/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13085365 BIOSIS Number: 99085365

IL-2 receptor gamma chain expression on CD34 positive hematopoietic progenitor cells from bone marrow and cord blood

Itano M; Tsuchiya S; Morita S; Fujie H; Ishii N; Yanagisawa T; Ohashi Y; Minegishi M; Sugamura K; Konno T
Dep. Pediatr. Oncol., Inst. Dev. Aging Cent., Tohoku Univ., Sendai 980-77, Japan

Tohoku Journal of Experimental Medicine 178 (4). 1996. 389-398.
Full Journal Title: Tohoku Journal of Experimental Medicine
ISSN: 0040-8727
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 004 Ref. 050814

The IL-2 receptor (IL-2R) gamma-chain is shared among receptors for IL-4, IL-7, IL-9 and IL-15 as well as IL-2. In order to clarify the functional role of these **cytokines** interacting with the common ychain in human

early hematopoiesis, we studied expression of the IL-2R ychain on purified CD34 positive cells from bone marrow and cord blood. Broad populations of bone marrow mononuclear cells were all found to express the IL-2R **gamma-chain** . CD34 positive cells were purified by CD34 monoclonal **antibodies** and immunomagnetic beads as representative hematopoietic progenitor cells. It was established that only 38 +- 10% of CD34 positive bone marrow cells (n=5) and 35+-12% of CD34 positive cord blood cells (n=11) expressed the IL-2R ychain. CD34(+) IL-2R gamma-chain(+) and CD34(+) IL-2R gamma-chain(-) cells fractionated by cell sorting were subjected to clonogenic assays that showed granulocyte-macrophage colony-forming cells (CFU-GM) were present evenly in both fractions, whereas erythroid burst-forming cells (BFU-E) were enriched in the CD34(+) IL-2R gamma-chain(-) fraction approximately two- to six-fold as compared with CD34(+) IL-2R gamma-chian(+) fraction. Such clonogenic features did not differ between the bone marrow and cord blood cases. These results indicate that CD34(+) IL-2R gamma-chain(-) cells contain immature cells already committed to the erythroid lineage.

3/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13030859 BIOSIS Number: 99030859
Tolerance induction to human gamma globulin in FcR gamma chain-deficient mice
Whitmer K J; Romball C G; Hobbs M V; Weigle W O
Scripps Res. Inst., La Jolla, CA 92037, USA
FASEB Journal 10 (6). 1996. A1179.
Full Journal Title: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists, New Orleans, Louisiana, USA, June 2-6, 1996. FASEB Journal
ISSN: 0892-6638
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 048 Iss. 007 Ref. 124595

3/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

12130126 BIOSIS Number: 98730126
Transcript synthesis and surface expression of the interleukin-2 receptor (alpha-, beta-, and gamma-chain) by normal and malignant myeloid cells
Schumann R R; Nakarai T; Gruss H-J; Brach M A; Von Arnim U; Kirschning C; Karawajew L; Ludwig W-D; Renauld J-C; Ritz J; Herrmann F
Humboldt Universitaet Berlin, Robert-Roessle Cancer Center, Lindenberger Weg 80, D-13122 Berlin, Germany
Blood 87 (6). 1996. 2419-2427.
Full Journal Title: Blood
ISSN: 0006-4971
Language: ENGLISH
Print Number: Biological Abstracts Vol. 101 Iss. 008 Ref. 114401
Expression of the interleukin-2 receptor alpha- (IL-2R-alpha), IL-2R-beta-, and the recently identified IL-2R-gamma-chain was examined on a wide range of cells of myeloid origin including neutrophils, monocytes, normal bone marrow-derived myeloid progenitors enriched for CD34+ cells, bone marrow blasts obtained from acute myelogenous leukemia (AML) patients, and permanent myeloid leukemia cell lines by reverse transcriptase-polymerase chain reaction and surface membrane analysis using receptor chain-specific monoclonal **antibodies** and flow cytometry. Expression of the p75 IL-2R-beta- and the p64 IL-2R-**gamma-chain** was a common finding in most of the myeloid cell samples investigated, whereas IL-2R-alpha-chain was less frequently expressed. Although the

high-affinity IL-2R form (i.e., the alpha+, beta+, gamma+ IL-2R form) was detectable in a small minority of primary AML samples as well as the KG-1 cell line and IL-2 binding to these cells was sufficient to initiate signal transduction as evidenced by an increase in overall protein tyrosine phosphorylation and more specifically in tyrosine phosphorylation of the Janus kinase (JAK) 3, in none of these cell types did exposure to IL-2 affect cell growth kinetics. These results suggest that, in myeloid cells, the IL-2R may not stimulate mitogenic responses or that its components may be expressed in a combinational association with receptors for other **cytokines** and that IL-2R-gamma may play a regulatory role in normal and malignant myelopoiesis possibly independent from IL-2. Because recent studies by others have indicated that the IL-2R-gamma- chain may be shared by the IL-4R, the IL-7R, and most likely the IL-9R, expression of mRNA of these receptor types was also investigated in these cell samples. Surprisingly, in a substantial part of the myeloid lineage cells examined, an IL-2R-gamma+, IL-4R-, IL-7R- configuration was noted that was, however, frequently associated with expression of IL-9R. Sharing of IL-9R/IL-2R components was furthermore suggested by inhibition of 125I-IL-2 binding to primary AML cells with excess of unlabeled IL-9.

3/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

12096203 BIOSIS Number: 98696203
Reduced expression of the interleukin-2-receptor gamma chain on cord blood lymphocytes: Relationship to functional immaturity of the neonatal immune response
Zola H; Fusco M; Weedon H; Macardle P J; Ridings J; Roberton D M
Child Health Res. Inst., Women's and Children's Hosp., 72 King William Rd., North Adelaide, SA 5006, Australia
Immunology 87 (1). 1996. 86-91.
Full Journal Title: Immunology
ISSN: 0019-2805
Language: ENGLISH
Print Number: Biological Abstracts Vol. 101 Iss. 007 Ref. 096484
Mutation of the interleukin-2 (IL-2) receptor y chain, which also serves as a component of the receptor complexes for IL-4, 7, 9 and 15, results in severe immune deficiency. We hypothesized that the immunological immaturity of healthy neonates might be associated with low levels of expression of this receptor molecule. Using monoclonal **antibody** and a highly sensitive immunofluorescence method, we showed that IL-2 receptor **gamma chain** is expressed at significantly lower levels on cord blood cells compared with adult cells. IL-2-dependent T-cell activation in vitro was reduced in cord blood cells compared with adult cells, but B-cell responses to IL-4 were not obviously impaired. The lower level of expression of the y chain and some other **cytokine** receptor chains may contribute to the immunological immaturity of the newborn, by selectively depressing particular immunological mechanisms.

3/7/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11796675 BIOSIS Number: 98396675
Production of a mouse anti-human interleukin-2 receptor **gamma chain** specific monoclonal **antibody**
Holmberg P; Oetken C; Raivio E; Lindqvist C
Abo Akademi Univ., Dep. Biochem, Abo, Finland
0 (0). 1995. 299.
Full Journal Title: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY. The 9th International Congress of Immunology; Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological

Societies, San Francisco, California, USA, July 23-29, 1995. ix+742p. 9th International Congress of Immunology: San Francisco, California, USA.
ISSN: *********
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 047 Iss. 009 Ref. 159078

3/7/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

7000825 BIOSIS Number: 87061346
IDENTIFICATION OF THE INTERLEUKIN-2 RECEPTOR IL-2R ON HUMAN LEUKEMIC T CELLS USING COLLOIDAL GOLD AND SCANNING ELECTRON MICROSCOPY
HELINSKI E H; BIELAT K L; OVAK G M; MEENAGHAN M A; WIRTH J E; PAULY J L
DEP. MOL. IMMUNOL., ROSWELL PARK MEML. INST., 666 ELM STREET, BUFFALO, N.Y. 14263.
J MED (WESTBURY) 19 (5-6). 1988. 353-368. CODEN: JNMDB
Full Journal Title: Journal of Medicine (Westbury)
Language: ENGLISH
Results of studies demonstrating the identification of the interleukin-2 receptor (IL-2R; i.e., anti-Tac) on the membrane ultra-structure of human leukemic T cells with an antibody carrying an electron dense colloidal gold microsphere (e.g., immiunogold) that was visualized using a scanning electron microscope (SEM) are reported. Our IL-2R model system employed HTLV-1 retrovirus-infected lymphoblastoid cells of the long-term human leukemic T cell line HUT-102B2. The presence of the IL-2R on these cells was defined using a double antibody procedure that employed as the primary atibody a purified mouse monoclonal anti-Leu-IL-2R **antibody** (mIgg1k, anti-Tac, CD25), and used as the secondary **antibody** a goat anti-mouse IgG (**gamma-chain** specific) **antibody** that had been covalently bonded to a 40 nm colloidal gold particle. More than 95% of the HUT-102B2 were IL-2R+, and there was a uniform distribution of the IL-2R over the surface of the cells. Corresponding controls were employed in all examination and included IL-2R Jurkat human leukemic T cells and isotype identical immunoglobulins. The primary and secondary antibody reagents contained whole human serum and bovine serum albumin, and there was no evidence of the non-specific binding of these antibodies. These studies are the first to demonstrate the presence of a lymphokine receptor on the surface architecture of a cell. We anticipate no difficulty in applying the immunogold/SEM technology to define both normal and malignant cell membrane receptors for other **cytokines**.

3/7/8 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

9758068 EMBASE No: 95314770
Characterization of the IL-6 responsive elements in the gamma fibrinogen gene promoter
Zhang Z.; Fuentes N.L.; Fuller G.M.
Dept. of Cell Biology, University of Alabama, Birmingham, AL 35294-0005 USA
Journal of Biological Chemistry (USA) , 1995, 270/41 (24287-24291)
CODEN: JBCHA ISSN: 0021-9258
LANGUAGES: English SUMMARY LANGUAGES: English
Fibrinogen, a hepatically derived class II acute phase protein, is the product of three separate genes, (Aalpha, Bbeta, and gamma). The fibrinogen genes are expressed constitutively; however, their transcription can he significantly up-regulated by interleukin-6 (IL-6) and glucocorticoid. Inspection of the promoter region of the fibrinogen gamma gene revealed three hexanucleotide clusters of CTGGGA that are recognized as class II IL-6 responsive elements. Functional analyses of these regions (designated here as site I, site II, and site III according to their position in the

promoter) were performed using luciferase reporter constructs and show a hierarchy of IL-6 response in which site II was the preferred functional site, site I was the next important site, and site III was the site least responsive to IL-6. Gel mobility shift assays using 25-base pair oligonucleotide probes derived from these three regions with the CTGGGA positioned in the middle and nuclear extracts from IL-6-treated primary hepatocytes reveal the presence of IL-6-induced high molecular weight complexes appearing 5 min after **cytokine** treatment. Supershift assays using anti-Stat3 **antibody** indicate that Stat3 is part of the IL-6-induced complex formed on the three **gamma chain** probes. The binding of Stat3 to the IL-6 responsive elements of the y probes is significantly weaker than to an alpha2-macroglobulin probe. These findings show for the first time that Stat3 is involved in associating with the IL-6 responsive elements of fibrinogen gamma chain, a class II acute phase gene other than alpha2- macroglobulin.

3/7/9 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

9398164 EMBASE No: 94336088
Expression of interleukin 2 receptors on human carcinoma cell lines and tumor growth inhibition by interleukin 2
Yasumura S.; Lin W.; Weidmann E.; Hebda P.; Whiteside T.L.
Pittsburgh Cancer Institute, W1041 Biomedical Science Tower, 211 Lothrop Street, Pittsburgh, PA 15213-2582 USA
INT. J. CANCER (USA) , 1994, 59/2 (225-234) CODEN: IJCNA ISSN: 0020-7136
LANGUAGES: English SUMMARY LANGUAGES: English
We have previously shown that human squamous cell carcinomas (SCC) express the interleukin 2 receptor (IL2R)-alpha and -beta chains, and that the ligand, IL2, directly inhibits growth of the tumor in vitro and in vivo in the tumor xenograft-nude mice model. We now show that the alpha and beta chains of IL2R are expressed on a variety of human carcinoma cell lines and on normal human keratinocytes in early-stage cultures. While all carcinoma cells in a population expressed IL2R-alpha and -beta proteins, in keratinocytes obtained from different normal donors, variable proportions of cells were positive, as measured by flow cytometry. The carcinoma lines and 2/5 keratinocyte lines studied were also found to contain transcripts for the IL2R-beta chain detectable by combined reverse transcription-PCR (RTPCR) and hybridization with the specific cDNA probe. Incubation of the gastric (HR) or renal cell carcinoma (RCC) cell lines but not of other IL2R+ carcinoma cell lines or normal keratino- cytes, in the presence of IL2 resulted in dose-dependent inhibition of tumor cell growth. Monoclonal **antibodies** (MAbs) specific for IL2R-**gamma chain** completely reversed this growth inhibitory effect of IL2. The ligand, IL2, also down-regulated surface expression of its own receptor and of intercellular adhesion molecule-I (ICAM-I) or class I major histocompatibility complex (MHC) antigens on IL2R+ tumor cells. All carcinoma cells studied incubated in the presence of IL2 exhibited significantly increased sensitivity to growth-inhibitory effects of other **cytokines** such as interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha or transforming growth factor (TGF)-beta IL2 inhibited growth of the HR cells by arresting a significant proportion of tumor cells in the G0/G1 phase of the cell cycle. Thus, IL2 can have direct effects on IL2R+ carcinoma cells, leading to changes in growth or to increases in sensitivity of tumor cells to cytostatic activities of other **cytokines**.

3/7/10 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

8760260 EMBASE No: 93063978
Principles of paramunization: Option and limits in veterinary medicine
Buttner M.
Institute of Medical Microbiology, Infectious and Epidemic Diseases, Veterinary Faculty, Univ of Munich, Veterinarstrasse 13, 8000 Munchen 22 Germany
COMP. IMMUNOL. MICROBIOL. INFECT. DIS. (United Kingdom) , 1993, 16/1 (1-10) CODEN: CIMID ISSN: 0147-9571
LANGUAGES: English SUMMARY LANGUAGES: English; French
The so-called primitive immune system has not changed during evolution. Even in primates it plays the most important role in first line defence against invading microorganisms. Cellular components such as macrophages, granulocytes, Natural Killer cells and gammadelta-T cells and soluble humoral factors - the **cytokines** - are the representants of the primitive immune system. An interlocking communicative network regulates flexible response of effector cells towards 'non-self' antigens. It also ensures close connection with the repertoire of specific immune response, e.g. antibody formation. Multifactorial diseases, nosocomial infections, tumour diseases and various forms of immunosuppression initiated alternative methods in immunotherapy. Immunostimulation at the nonspecific defence level has first been noticed as 'side effects' of vaccination. Today it should be differentiated between substitution of the immune system with **cytokines** and induction of the non-specific defence repertoire mimicking natural antigen contact that is called paramunization. Advantages and disadvantages of both methods are discussed. In vitro as well as in vivo experiments with poxviruses document safety and efficacy of purified and inactivated virus particles in paramunization protocols. The main stimulative components of the poxvirus particles are located in the envelope of the virions. Poxvirus-induced stimulation of non-specific defence reactions is likely to have remote effects on the quality of further antigen processing. Besides the induction of a high short-term alertness in the primitive immune system paramunization may efficiently influence ongoing specific responses, e.g. immunoglobulin isotype selection. Therefore the term paramunization should not be used to characterize a separate part of the immune system, however, for didactic reasons it will facilitate the understanding of principles of the immune system.

3/7/11 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

06677496 90304313
Receptor expression and functional status of cultured human eosinophils derived from umbilical cord blood mononuclear cells.
Walsh GM; Hartnell A; Moqbel R; Cromwell O; Nagy L; Bradley B; Furitsu T; Ishizaka T; Kay AB
Department of Allergy and Clinical Immunology, National Heart and Lung Institute, London, UK.
Blood (UNITED STATES) Jul 1 1990, 76 (1) p105-11, ISSN 0006-4971 Journal Code: A8G
Contract/Grant No.: AI-10060, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Selective use of recombinant human **cytokines** has enabled the culture of large numbers of eosinophils from human cord blood mononuclear cells, raising the possibility of their use as a model of eosinophil function. Cultured eosinophils (CE) were compared with normal-density peripheral blood eosinophils (PBE) in terms of their membrane receptor expression and function. Fc gamma R and CR1 expression of CE and PBE was similar. In contrast, the specific mean fluorescence for LFA-1 alpha, p150,95 alpha, ICAM-1, and HLA-DR was significantly elevated for CE compared with PBE. CE responded in PAF-induced chemotaxis in a similar fashion to PBE. CE gave higher numbers of both resting and platelet

activating factor (PAF)-stimulated immunoglobulin G (IgG)- and C3b-dependent rosettes than PBE. CE and PBE had comparable capacity to kill IgG- and C-opsonized schistosomula in terms of both baseline values and PAF-induced enhancement of cytotoxicity. Baseline adherence by CE and PBE to plasma-coated glass was essentially the same, but stimulated adhesion (PAF) of CE was lower. Compared with PBE, CE generated less than half the amounts of extracellular and cell-associated PAF induced by calcium ionophore A23187 stimulation. Unlike PBE, CE did not generate PAF after exposure to IgG-coated Sepharose particles. CE stimulated with IgG-coated beads generated small quantities of LTC4, while A23187 stimulation resulted in approximately half the LTC4 levels observed with PBE. The total cell content of eosinophil peroxidase (EPO) was similar for CE and PBE. These data suggest that although CE and PBE have many phenotypic and functional properties in common there are quantitative differences that may be a consequence of their immaturity and/or the influence of the **cytokines** used in their culture.

3/7/12 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127016508 CA: 127(2)16508y PATENT
T cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
INVENTOR(AUTHOR): Boussiotis, Vassiliki A.; Nadler, Lee M.
LOCATION: USA
ASSIGNEE: Dana-Farber Cancer Institute
PATENT: PCT International ; WO 9717360 A2 DATE: 19970515
APPLICATION: WO 96US17927 (19961112) *US 556038 (19951109)
PAGES: 45 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-000/A
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215005 Immunochemistry
CA201XXX Pharmacology
IDENTIFIERS: T cell anergy regulation cytokine receptor, autoimmune disease treatment cytokine receptor modulator, interleukin T cell anergy regulation
DESCRIPTORS:
Alloantigens... Antibodies... Antigens... Autoantigens... Tumor-associated antigen...
agents that stimulating .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Pathogenic bacteria...
antigens that stimulating .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Cytokine receptors... Interleukin 2 receptors... Interleukin 4 receptors... Interleukin 7 receptors...
.gamma.-chain regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Interleukin receptors...
interleukin 15 receptors, .gamma.-chain regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Parasite... Virus...
pathogenic, antigens that stimulating .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Interleukin 15...
receptors, .gamma.-chain regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine

receptor .gamma.-chains
T-cell lymphopoiesis...
regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Anergy... Drug screening... Immunotherapy... Interleukin 15... Interleukin 2... Interleukin 4... Interleukin 7...
t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Autoimmune diseases... Graft-vs.-host reaction...
treatment; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
CAS REGISTRY NUMBERS:
157482-36-5 phosphorylation and assocn. with cytokine receptor .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains

3/7/13 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

125084121 CA: 125(7)84121a JOURNAL
Single chain Ig/.gamma. gene-redirected human T lymphocytes produce cytokines, specifically lyse tumor cells, and recycle lytic capacity
AUTHOR(S): Weijtens, Mo E. M.; Willemsen, Ralph A.; Valerio, Dinko; Stam, Kees; Bolhuis, Reinder L. H.
LOCATION: Department Clinical Tumor Immunology, Daniel Hoed Cancer Center , Rotterdam, Neth.
JOURNAL: J. Immunol. DATE: 1996 VOLUME: 157 NUMBER: 2 PAGES: 836-843
CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English
SECTION:
CA215003 Immunochemistry
IDENTIFIERS: tumor lysis T lymphocyte gene transduction, IgE Fc receptor antibody transduction lymphocyte
DESCRIPTORS:
Lymphokines and Cytokines,tumor necrosis factor-.alpha....
cytokine formation by human T lymphocytes that have have a chimeric gene that encodes a single chain monoclonal antibody-IgE Fc receptor mol.
Immunoglobulin receptors,Fc.epsilon.RI (IgE fragment Fc receptor I)...
Receptors,Fc.epsilon.RI (IgE fragment Fc receptor I)...
.gamma. chain; retrovirus-mediated transduction with a chimeric gene that encodes a single chain monoclonal antibody-IgE Fc receptor mol. stimulates human T lymphocytes to specifically lyse tumor cell
Therapeutics,geno-...
retrovirus-mediated transduction of T-cells with a chimeric gene that encodes a single chain monoclonal antibody-IgE Fc receptor mol. in relation to
Kidney,neoplasm, renal cell carcinoma... Lymphocyte,T-cell, cytotoxic... Neoplasm...
retrovirus-mediated transduction with a chimeric gene that encodes a single chain Ig-IgE Fc receptor mol. stimulates human T lymphocytes to specifically lyse tumor cells
Antibodies,monoclonal... Cytolysis... Gene,animal, chimeric... Transduction,genetic... Virus,animal, retro-...
retrovirus-mediated transduction with a chimeric gene that encodes a single chain monoclonal antibody-IgE Fc receptor mol. stimulates human T lymphocytes to specifically lyse tumor cells
CAS REGISTRY NUMBERS:
83869-56-1 cytokine formation by human T lymphocytes that have have a chimeric gene that encodes a single chain monoclonal antibody-IgE Fc receptor mol.

3/7/14 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124200210 CA: 124(15)200210j PATENT
Methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
INVENTOR(AUTHOR): Boussiotis, Vassiliki A.; Nadler, Lee M.
LOCATION: USA
ASSIGNEE: Dana-Farber Cancer Institute
PATENT: PCT International ; WO 9601122 A1 DATE: 960118
APPLICATION: WO 95US8320 (950630) *US 270152 (940701)
PAGES: 38 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/20A; A61K-039/395B; A61K-039/12B; A61K-039/02B; A61K-039/002B; A61K-039/00B; G01N-033/53B; G01N-033/68B; A61K-039/12J; A61K-038/20J; A61K-039/02K; A61K-038/20K; A61K-039/002L; A61K-038/20L; A61K-039/00M; A61K-038/20M
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215005 Immunochemistry
IDENTIFIERS: T lymphocyte hematopoiesis cytokine receptor gamma, interleukin 2 4 7 JAK kinase
DESCRIPTORS:
Lymphokine and cytokine receptors... Receptors,cytokine...
.gamma. chain; methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
Antigens... Antigens,allo-... Antigens,auto-... Antigens,tumor-assocd.... Autoimmune disease... Bacteria... Bone marrow,transplant... Hematopoiesis,T-cell lymphopoiesis... Lymphokine and cytokine receptors,interleukin 2... Lymphokine and cytokine receptors,interleukin 4 ... Lymphokine and cytokine receptors,interleukin 7... Lymphokines and Cytokines... Lymphokines and Cytokines,interleukin 2... Lymphokines and Cytokines,interleukin 4... Lymphokines and Cytokines,interleukin 7... Microorganism,pathogenic... Parasite... Receptors,interleukin 2... Receptors,interleukin 4... Receptors,interleukin 7... Transplant and Transplantation,allo-... Transplant and Transplantation,graft-vs.-host reaction... Transplant and Transplantation,xeno-... Virus...
methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
Antibodies...
to cytokine receptor .gamma. chain; methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
CAS REGISTRY NUMBERS:
161384-16-3 methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain

3/7/15 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

123110161 CA: 123(9)110161u PATENT
Antibody to human interleukin 2 receptor as immunosuppressant or anti-allergic agent
INVENTOR(AUTHOR): Shimamura, Toshiaki; Taki, Shinsuke; Hamuro, Junji; Sugamura, Kazuo; Takeshita, Toshiichi; Kondo, Motonari
LOCATION: Japan,
ASSIGNEE: Ajinomoto Kk; Sugamura Kazuo
PATENT: Japan Kokai Tokkyo Koho ; JP 95149662 A2 ; JP 07149662 DATE: 950613
APPLICATION: JP 94213706 (940907) *JP 93223574 (930908)
PAGES: 11 pp. CODEN: JKXXAF LANGUAGE: Japanese CLASS: A61K-039/395A
SECTION:
CA215003 Immunochemistry
IDENTIFIERS: interleukin 2 receptor gamma chain antibody,

immunosuppressant antiallergic monoclonal antibody IL2 receptor
DESCRIPTORS:
Allergy inhibitors... Antibodies,monoclonal...
Glycophosphoproteins,interleukin 2-binding, p64... Immunosuppressants...
Lymphokines and Cytokines,interleukin 4...
monoclonal antibody to human interleukin 2 receptor .gamma. chain as immunosuppressant or anti-allergic agent that inhibits interleukin 4-mediated disorder or allergy

3/7/16 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122158626 CA: 122(13)158626f PATENT
A monoclonal antibody to the interleukin 2 receptor .gamma. chain for use as an immunosuppressant
INVENTOR(AUTHOR): Shimamura, Toshiro; Hamura, Junji; Nakazawa, Harumi; Kanayama, Yuka; Sugamura, Kazuo; Takeshita, Toshikazu
LOCATION: Japan,
ASSIGNEE: Ajinomoto Co., Inc.
PATENT: European Pat. Appl. ; EP 621338 A2 DATE: 941026
APPLICATION: EP 94106257 (940421) *JP 9394491 (930421) *JP 9436065 (940307)
PAGES: 37 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C12N-015/13A; C12P-021/08B; C12N-005/20B; A61K-039/395B; C12N-001/21B; C12N-005/10B; C12P-021/00B DESIGNATED COUNTRIES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
SECTION:
CA215003 Immunochemistry
CA201XXX Pharmacology
IDENTIFIERS: interleukin 2 receptor monoclonal antibody immunosuppressant
DESCRIPTORS:
Allergy inhibitors... Antibodies,monoclonal... Immunosuppressants...
Inflammation inhibitors... Lymphokine and cytokine receptors,interleukin 2 ... Receptors,interleukin 2...
a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for use as an immunosuppressant
Gene,animal...
cDNA; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for use as an immunosuppressant
Deoxyribonucleic acid sequences,complementary...
for fusion of proteins of light and heavy chains of monoclonal antibodies to human interleukin 2 receptor .gamma. subunit; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for u
Protein sequences...
of fusion of proteins of light and heavy chains of monoclonal antibodies to human interleukin 2 receptor .gamma. subunit; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for us
Plasmid and Episome...
pFv(GP-2)-DE, pFv(GP-4)-DE, cDNAs for Fv fragments of monoclonal antibody to .gamma. subunit of human interleukin 2 receptor; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain fo
Plasmid and Episome...
pIL2-RGS, cDNA for .gamma. subunit of human interleukin 2 receptor on, expression in Escherichia coli of; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for use as an immunosu
Autoimmune disease... Transplant and Transplantation,graft-vs.-host reaction...
treatment of; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for use as an immunosuppressant
CAS REGISTRY NUMBERS:

161309-68-8 161309-69-9 amino acid sequence; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for use as an immunosuppressant
161309-70-2 161309-71-3 nucleotide sequence; a monoclonal antibody to the human interleukin 2 receptor .gamma. chain for use as an immunosuppressant

3/7/17 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

120268217 CA: 120(21)268217q PATENT
Cloning and expression of cDNA for human interleukin-2 receptor gamma chain
INVENTOR(AUTHOR): Sugamura, Kazuo; Takeshita, Toshikazu; Asao, Hironobu; Nakamura, Masataka; Shimamura, Toshiro; Suzuki, Manabu; Hamuro, Junji
LOCATION: Japan,
ASSIGNEE: Ajinomoto Co., Inc.
PATENT: European Pat. Appl. ; EP 578932 A2 DATE: 940119
APPLICATION: EP 93106561 (930422) *JP 92104947 (920423)
PAGES: 50 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C12N-015/12A; C07K-013/00B; C12P-021/08B; C12N-005/10B; G01N-033/48B; G01N-033/577B; A61K-037/02B; A61K-039/395B; A61K-039/44B DESIGNATED COUNTRIES: DE; FR; GB ; IT
SECTION:
CA215005 Immunochemistry
CA203XXX Biochemical Genetics
IDENTIFIERS: interleukin 2 receptor gamma chain cDNA, cloning IL2 receptor gamma chain cDNA
DESCRIPTORS:
Gene,animal...
cDNA, for interleukin-2 receptor gamma chain of human, cloning and expression of
Animal cell line,CHO... Animal cell line,L-929... Escherichia coli... Eukaryote... Prokaryote...
expression in, cDNA for human interleukin-2 receptor gamma chain for
Deoxyribonucleic acid sequences,complementary...
for interleukin-2 receptor gamma chain of human
Lymphokines and Cytokines,interleukin 2, receptors... Receptors,interleukin 2...
gamma chain of, cDNA for, of human, cloning and expression of
Immunomodulators...
human interleukin-2 receptor gamma chain and its antibody as
Protein sequences...
of interleukin-2 receptor gamma chain of human
Antibodies... Antibodies,monoclonal...
to human interleukin-2 receptor gamma chain, prepn. of
CAS REGISTRY NUMBERS:
148348-31-6 154609-72-0 amino acid sequence of and cloning and expression of cDNA for
154609-71-9 154609-73-1 154609-74-2 154609-75-3 154609-76-4 nucleotide sequence and cloning of

```
? e au=boussiotis

 Ref    Items  Index-term
 E1         2  AU=BOUSSIOS, T.
 E2        16  AU=BOUSSIOS, THALIA
 E3         0 *AU=BOUSSIOTIS
 E4        11  AU=BOUSSIOTIS V
 E5        71  AU=BOUSSIOTIS V A
 E6         1  AU=BOUSSIOTIS V.
 E7        44  AU=BOUSSIOTIS V.A.
 E8        39  AU=BOUSSIOTIS VA
 E9         1  AU=BOUSSIOTIS, V. A.
 E10        2  AU=BOUSSIOTIS, VASSILIKI
 E11       23  AU=BOUSSIOTIS, VASSILIKI A.
 E12        2  AU=BOUSSIOTIS, VICKI A.

           Enter P or PAGE for more
? p

 Ref    Items  Index-term
 E13        5  AU=BOUSSIOTIS, VIKI A.
 E14        1  AU=BOUSSIOTOY A
 E15       10  AU=BOUSSIOU M
 E16        4  AU=BOUSSIOU M.
 E17        1  AU=BOUSSIOU P
 E18        1  AU=BOUSSIOU P.
 E19        2  AU=BOUSSIOU, M.
 E20        4  AU=BOUSSIOUD-CORBIERES F
 E21        1  AU=BOUSSIOUTIS, VASSILIKI A.
 E22        1  AU=BOUSSIOUX A
 E23        6  AU=BOUSSIOUX A M
 E24        6  AU=BOUSSIOUX A.-M.

           Enter P or PAGE for more
? s e4-e11

              11  AU=BOUSSIOTIS V
              71  AU=BOUSSIOTIS V A
               1  AU=BOUSSIOTIS V.
              44  AU=BOUSSIOTIS V.A.
              39  AU=BOUSSIOTIS VA
               1  AU=BOUSSIOTIS, V. A.
               2  AU=BOUSSIOTIS, VASSILIKI
              23  AU=BOUSSIOTIS, VASSILIKI A.
      S4     191  E4-E11
? s s4 and (gamma(w)chain

>>>Unmatched parentheses
? s s4 and gamma(w)chain

             191  S4
          516643  GAMMA
          678765  CHAIN
            6405  GAMMA(W)CHAIN
      S5      18  S4 AND GAMMA(W)CHAIN
? rd s5
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>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S6 10 RD S5 (unique items)
? t s6/7/all

6/7/1 (Item 1 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13090260 BIOSIS Number: 99090260
Pre-B acute lymphoblastic leukemia cells may induce T-cell anergy to alloantigen
Cardoso A A; Schultze J L; **Boussiotis V A**; Freeman G J; Seamon M J; Laszlo S; Billet A; Sallan S E; Gribben J G; Nadler L M
Dana-Farber Cancer Inst., D-740, 44 Binney St. Boston, MA 02115, USA
Blood 88 (1). 1996. 41-48.
Full Journal Title: Blood
ISSN: 0006-4971
Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 004 Ref. 055709
Even if neoplastic cells express tumor associated antigens they still may fail to function as antigen presenting cells (APC) if they lack expression of one or more molecules critical for the induction of productive immunity. These cellular defects can be repaired by physiologic activation, transfection, or fusion of tumor cells with professional APC. Although such defects can be repaired, antitumor specific T cells may still fail to respond in vivo if they may have been tolerized. Here, human pre-B cell acute lymphoblastic leukemia (pre-B ALL) was used as a model to determine if primary human tumor cells can function as alloantigen presenting cells (alloAPC) or alternatively whether they induce energy. In the present report, we show that pre-B cell ALL express alloantigen and adhesion molecules but uniformly lack B7-1 (CD80) and only a subset express B7-2 (CD86). Pre-B ALL cells are inefficient or ineffective alloAPC and those cases that lack expression of B7-1 and B7-2 also induce alloantigen specific T-cell unresponsiveness. Under these circumstances, T-cell unresponsiveness could be prevented by physiologic activation of tumor cells via CD40, cross-linking CD28, or signaling through the common **gamma chain** of the interleukin-2 receptor on T cells. Taken together, these results suggest that pre-B ALL may be incapable of inducing clinically significant T-cell-mediated antileukemia responses. This defect may be not only due to their inability to function as APC, but also due to their potential to induce tolerance. Attempts to induce clinically significant antitumor immune responses may then require not only mechanisms to repair the antigen presenting capacity of the tumor cells, but also reversal of tolerance.

6/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

13039673 BIOSIS Number: 99039673
Complete blockade of B7 family-mediated costimulation is necessary to induce human alloantigen-specific anergy: A method to ameliorate graft-versus-host disease and extend the donor pool
Gribben J G; Guinan E C; **Boussiotis V A**; Ke X-Y; Linsle L; Sieff C; Gray G S; Freeman G J; Nadler L M
Div. Hematol. Malignancies, Dana-Farber Cancer Inst., 44 Binney St., Boston, MA 02115, USA
Blood 87 (11). 1996. 4887-4893.
Full Journal Title: Blood
ISSN: 0006-4971

Language: ENGLISH
Print Number: Biological Abstracts Vol. 102 Iss. 002 Ref. 021846
Graft-versus-host disease (GVHD) is initiated by adoptively transferred donor T cells that recognize host alloantigens. Whereas the absence of donor T-cell proliferation to host alloantigens in a mixed-leukocyte reaction does not predict freedom from GVHD, the frequency of alloreactive precursor helper T lymphocytes (pHTL) is predictive. Complete blockade of B7 family-mediated costimulation, but not of major histocompatibility complex recognition or adhesion, induces host alloantigen-specific energy by reducing cytokine production below threshold levels necessary for common **gamma-chain** signaling. The associated reduction of alloreactive pHTL frequency below that predictive for GVHD, without depletion of either nonallospecific T cells or hematopoietic progenitors, has led us to embark upon human clinical trials of haplomismatched allogeneic bone marrow transplantation.

6/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11941641 BIOSIS Number: 98541641
The critical role of CD28 signalling in the prevention of human T-cell anergy
Boussiotis V A; Freeman G J; Gribben J G; Nadler L M
Div. Hematol. Malignancies, Dana Farber Cancer Inst., Harv. Med. Sch., Boston, MA 02115, USA
Research in Immunology 146 (3). 1995. 140-149.
Full Journal Title: Research in Immunology
ISSN: 0923-2494
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 012 Ref. 178332

6/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11469081 BIOSIS Number: 98069081
Common **gamma-chain** signaling is sufficient to prevent alloantigen specific T-cell clonal anergy
Boussiotis V A; Barber D L; Nakarai T; Freeman G J; Gribben J G; Bernstein G M; D'Andrea A D; Ritz J; Nadler L M
Div. Hematologic Malignancies Pediatric Oncol., Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA, USA
Blood 84 (10 SUPPL. 1). 1994. 111A.
Full Journal Title: Abstracts Submitted to the 36th Annual Meeting of the American Society of Hematology, Nashville, Tennessee, USA, December 2-6, 1994. Blood
ISSN: 0006-4971
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 047 Iss. 002 Ref. 030668

6/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11435459 BIOSIS Number: 98035459
Prevention of T cell anergy by signaling through the gamma-c chain of the IL-2 receptor
Boussiotis V A; Barber D L; Nakarai T; Freeman G J; Gribben J G; Bernstein G M; D'Andrea A D; Ritz J; Nadler L M
Div. Hematol. Malignancies, Dana-Farber Cancer Inst., Harvard Sch., Boston, MA 02115, USA

Science (Washington D C) 266 (5187). 1994. 1039-1042.
Full Journal Title: Science (Washington D C)
ISSN: 0036-8075
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 002 Ref. 020003
When stimulated through their antigen receptor without requisite costimulation, T cells enter a state of antigen-specific unresponsiveness, termed anergy. In this study, signaling through the common **gamma chain** of the interleukin-2 (IL-2), IL-4, and IL-7 receptors in the presence of antigen was found to be sufficient to prevent the induction of anergy. After culture with IL-2, IL-4, or IL-7, Jak3 kinase was tyrosine-phosphorylated, which correlated with the prevention of anergy. Therefore, a signal through the common **gamma chain** may regulate the decision of T cells to either clonally expand or enter a state of anergy.

6/7/6 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

9616444 EMBASE No: 95171678
B7-1 and B7-2 do not deliver identical costimulatory signals, since B7-2 but not B7-1 preferentially costimulates the initial production of IL-4
Freeman G.J.; **Boussiotis V.A.**; Anumanthan A.; Bernstein G.M.; Ke X.-Y.; Rennert P.D.; Gray G.S.; Gribben J.G.; Nadler L.M.
Dana-Farber Cancer Institute, Department of Medicine, Harvard Medical School, Boston, MA 02115 USA
Immunity (USA) , 1995, 2/5 (523-532) CODEN: IUNIE ISSN: 1074-7613
LANGUAGES: English SUMMARY LANGUAGES: English
The functional necessity for two CD28 counterreceptors (B7-1 and B7-2) is presently unknown. B7-1 and B7-2 equivalently costimulate IL-2 and interferon-gamma (IFNgamma) production and IL-2 receptor alpha and **gamma chain** expression. B7-2 induces significantly more IL-4 production than B7-1, with the greatest difference seen in naive T cells. Repetitive costimulation of CD4+CD45RA+ T cells with B7-2 results in moderate levels of both IL-4 and IL-2, whereas repetitive costimulation with B7-1 results in high levels of IL-2 and low levels of IL-4. Therefore, B7-1 and B7-2 costimulation mediate distinct outcomes, since B7-2 provides an initial signal to induce naive T cells to become IL-4 producers, thereby directing the immune response more towards Th0/Th2, whereas B7-1 is a more neutral differentiative signal.

6/7/7 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

127016508 CA: 127(2)16508y PATENT
T cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
INVENTOR(AUTHOR): Boussiotis, Vassiliki A.; Nadler, Lee M.
LOCATION: USA
ASSIGNEE: Dana-Farber Cancer Institute
PATENT: PCT International ; WO 9717360 A2 DATE: 19970515
APPLICATION: WO 96US17927 (19961112) *US 556038 (19951109)
PAGES: 45 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-000/A
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215005 Immunochemistry
CA201XXX Pharmacology
IDENTIFIERS: T cell anergy regulation cytokine receptor, autoimmune disease treatment cytokine receptor modulator, interleukin T cell anergy regulation

DESCRIPTORS:
Alloantigens... Antibodies... Antigens... Autoantigens... Tumor-associated antigen...
agents that stimulating .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Pathogenic bacteria...
antigens that stimulating .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Cytokine receptors... Interleukin 2 receptors... Interleukin 4 receptors... Interleukin 7 receptors...
.gamma.-chain regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Interleukin receptors...
interleukin 15 receptors, .gamma.-chain regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Parasite... Virus...
pathogenic, antigens that stimulating .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Interleukin 15...
receptors, .gamma.-chain regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
T-cell lymphopoiesis...
regulation; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Anergy... Drug screening... Immunotherapy... Interleukin 15... Interleukin 2... Interleukin 4... Interleukin 7...
t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
Autoimmune diseases... Graft-vs.-host reaction...
treatment; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains
CAS REGISTRY NUMBERS:
157482-36-5 phosphorylation and assocn. with cytokine receptor .gamma.-chain; t cell proliferation and anergy regulation by interleukins or other agents that stimulate cytokine receptor .gamma.-chains

6/7/8 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124200210 CA: 124(15)200210j PATENT
Methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
INVENTOR(AUTHOR): Boussiotis, Vassiliki A.; Nadler, Lee M.
LOCATION: USA
ASSIGNEE: Dana-Farber Cancer Institute
PATENT: PCT International ; WO 9601122 A1 DATE: 960118
APPLICATION: WO 95US8320 (950630) *US 270152 (940701)
PAGES: 38 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/20A; A61K-039/395B; A61K-039/12B; A61K-039/02B; A61K-039/002B; A61K-039/00B; G01N-033/53B; G01N-033/68B; A61K-039/12J; A61K-038/20J; A61K-039/02K; A61K-038/20K; A61K-039/002L; A61K-038/20L; A61K-039/00M; A61K-038/20M
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215005 Immunochemistry
IDENTIFIERS: T lymphocyte hematopoiesis cytokine receptor gamma,

interleukin 2 4 7 JAK kinase
DESCRIPTORS:
Lymphokine and cytokine receptors... Receptors,cytokine...
.gamma. chain; methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
Antigens... Antigens,allo-... Antigens,auto-... Antigens,tumor-assocd.... Autoimmune disease... Bacteria... Bone marrow,transplant... Hematopoiesis,T-cell lymphopoiesis... Lymphokine and cytokine receptors,interleukin 2... Lymphokine and cytokine receptors,interleukin 4 ... Lymphokine and cytokine receptors,interleukin 7... Lymphokines and Cytokines... Lymphokines and Cytokines,interleukin 2... Lymphokines and Cytokines,interleukin 4... Lymphokines and Cytokines,interleukin 7... Microorganism,pathogenic... Parasite... Receptors,interleukin 2... Receptors,interleukin 4... Receptors,interleukin 7... Transplant and Transplantation,allo-... Transplant and Transplantation,graft-vs.-host reaction... Transplant and Transplantation,xeno-... Virus...
methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
Antibodies...
to cytokine receptor .gamma. chain; methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain
CAS REGISTRY NUMBERS:
161384-16-3 methods for modulating T cell responses by manipulating a common cytokine receptor gamma chain

6/7/9 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

011303072 **Image available**
WPI Acc No: 97-280977/199725
Stimulating or inhibiting proliferation of T cells expressing cytokine receptor **gamma chain** - comprises treatment with e.g. antibody that binds to this chain, useful for treatment of e.g. auto-immune disease, transplant rejection and guest versus host diseases
Patent Assignee: DANA FARBER CANCER INST INC (DAND)
Inventor: **BOUSSIOTIS V A**; NADLER L M
Number of Countries: 020 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9717360	A2	19970515	WO 96US17927	A	19961112		199725 B
AU 9710506	A	19970529	AU 9710506	A	19961112		199737

Priority Applications (No Type Date): US 95556038 A 19951109
Cited Patents: No-SR.Pub
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9717360	A2	E	46			

Designated States (National): AU CA JP
Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

AU 9710506	A	Based on	WO 9717360

Abstract (Basic): WO 9717360 A
Stimulating proliferation of T cells that express a cytokine receptor **gamma chain** (A), and which have received a primary activating signal under conditions that normally result in unresponsiveness comprises treating the T cells with an agent (I) that binds (A) and stimulates an intracellular signal in the cell that causes proliferation. (I) is not natural interleukin (IL)-2. Also new are: (1) induction of unresponsiveness to an antigen (Ag) in a T cell that expresses (A) by contacting it, in presence of Ag, with an agent (II) that inhibits delivery of a signal through (A); (2) a method for identifying (II).

USE - Induction of unresponsiveness is useful for treating a wide variety of autoimmune diseases, transplant rejection, unwanted immune responses such as allergies and especially graft versus host disease in patients given bone marrow transplants. Inducing proliferation is also used to improve the response to a vaccinating Ag, derived from a microorganism or tumour.

Dwg.1/11

Derwent Class: B04

International Patent Class (Main): C07K-000/00; C07K-014/00

6/7/10 (Item 2 from file: 351)

DIALOG(R)File 351:DERWENT WPI

010590567 **Image available**

WPI Acc No: 96-087520/199609

Modulation of T cell responses with therapeutic applications - by manipulating a common cytokine receptor **gamma chain**

Patent Assignee: DANA FARBER CANCER INST INC (DAND)

Inventor: **BOUSSIOTIS V A**; NADLER L M

Number of Countries: 020 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
WO 9601122	A1	19960118	WO 95US8320	A	19950630	A61K-038/20	199609 B
AU 9529152	A	19960125	AU 9529152	A	19950630	A61K-038/20	199618
EP 768890	A1	19970423	EP 95924766	A	19950630	A61K-038/20	199721
			WO 95US8320	A	19950630		

Priority Applications (No Type Date): US 94270152 A 19940701

Cited Patents: 06Jnl.Ref; EP 621338

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
WO 9601122	A1	E	39			
Designated States (National): AU CA JP						
Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE						
AU 9529152	A			Based on		WO 9601122
EP 768890	A1	E		Based on		WO 9601122
Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE						

Abstract (Basic): WO 9601122 A

The following are claimed: (A) a method for stimulating proliferation by a T cell which expresses a cytokine receptor **gamma-chain** and which has received a prim. activation signal under conditions, which normally result in no response in a T cell, comprises contacting the T cell with an agent (I) which binds to the cytokine receptor **gamma-chain** and stimulates an intracellular signal in the T cell resulting in T cell proliferation, provided that (I) does not consist of natural interleukin (Il)-2; (B) a method in which (I) acts intracellularly to stimulate phosphorylation of a JAK kinase with a mol.wt. of about 116kD as determined by SDS polyacrylamide gel electrophoresis, resulting in proliferation of the T cell; (C) a method for inducing no response to an antigen (Ag) in a T cell which expresses a cytokine receptor **gamma-chain**, comprising contacting the T cell in the presence of an Ag with an agent (II), which inhibits delivery of a signal through the cytokine receptor **gamma-chain**, resulting in T cell no response to the antigen; (D) a method for inhibiting graft-versus-host disease (GVHD) in a bone marrow transplant recipient by contacting a donor T cell, which expresses a cytokine receptor **gamma-chain**, with a cell which expresses a recipient Ag and (II), resulting in donor T cell no response to the cell which expresses the recipient Ag; and (E) a method for identifying (II) comprising (a) contacting a T cell which expresses

a cytokine receptor **gamma-chain** with (1) a first agent which stimulates a prim. activation signal in the T cell, (2) a second agent which stimulates an intracellular signal through the cytokine receptor **gamma-chain** and (3) a third agent to be tested for the ability to inhibit delivery of the signal through the cytokine receptor **gamma-chain**, and (b) determining the presence of T cell proliferation, in which inhibition of T cell proliferation indicates that the third agent inhibits delivery of a signal to T cell through the cytokine receptor **gamma-chain**.

USE - (I) may be used to enhance an anti-tumour response or a T-cell response to pathogens, such as viruses, bacteria, fungi and parasites. (I) may also be used to increase the efficacy of vaccination. (II) may be used to prevent organ transplant rejection and to inhibit GVHD, to treat autoimmune diseases such as diabetes mellitus, arthritis, multiple sclerosis, SLE, dermatitis, psoriasis, Sjogren's Syndrome, alopecia areata, Crohn's disease, asthma and vaginitis, to treat allergy and allergic reactions and to energise T cells responsive to a therapeutic antibody (Ab).

Dwg.1/4

Derwent Class: B04; D16; S03

International Patent Class (Main): A61K-038/20

International Patent Class (Additional): A61K-039/00; A61K-039/002; A61K-039/02; A61K-039/12; A61K-039/395; G01N-033/53; G01N-033/68; A61K-038-20